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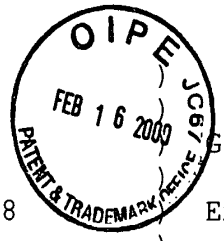
1803 PATENT
Attorney Docket No: 03495-0008-08

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES



In re application of)
)
Marc ALIZON et al.) Group Art Unit: 1648
)
Serial No.: 08/384,248) Examiner: J. PARKIN
)
Filed: February 6, 1995)
)
For: METHOD OF PRODUCING)
ANTIBODIES TO ANTIGENS)
OF HUMAN)
IMMUNODEFICIENCY)
VIRUS TYPE 1 (HIV 1))

Assistant Commissioner for Patents
Washington, D.C. 20231

REPLY BRIEF

In response to the Examiner's Answer dated December 20, 1999, appellants submit the following remarks.

REMARKS

1. Issues Resolved by Examiner's Answer

In the Examiner's Answer dated December 20, 1999, the Examiner stated: "The summary of invention contained in the brief is correct." and "The appellants' statement of the issues in the brief is correct." (Examiner's Answer at 2.) Accordingly, the Examiner does not dispute the accuracy of these sections of the Brief. The Examiner's agreement with

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appellants' portrayal of the invention and the issues thus resolves several issues.

First, the Examiner agrees that HIV-1 antigens and antibodies against the antigens were known at the time of appellants' invention. The Examiner also agrees that little was known about the molecular biology of the virus, including those regions of the genome that encoded polypeptides that had antigenic properties. The Examiner further agrees that appellants were the first to create a recombinant molecular clone of the genome of HIV-1. Consequently, it is undisputed that appellants possessed the first recombinant molecular clone of the genome of HIV-1.

Second, the Examiner agrees that this HIV-1 molecular clone enabled appellants to elucidate some of the structural features of the virus. The Examiner also agrees that appellants discovered that the HIV-1 molecular clone contained several restriction sites that were related to the *env*, *pol*, and *gag* genes, including: a *Kpn*I site at about 6100 and a *Bgl*II site at about 9150, a *Kpn*I site at about 3500 and a *Bgl*II site at about 6500, and a *Pst*I site at about 800 and a *Kpn*I site at about 3500. The Examiner agrees that these restriction fragments are

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recited in the claims on appeal. It is undisputed that appellants possessed the claimed restriction fragments.

Third, the Examiner agrees that appellants believed the claimed restriction fragments encoded at least part of the *env*, *pol*, and *gag* genes, respectively. The Examiner also agrees that the claimed restriction fragments do, in fact, code for proteins and polypeptides. Consequently, it is undisputed that the claimed restriction fragments encode proteins and polypeptides.

Fourth, the Examiner concedes that the skilled artisan, at the time that the application was filed, provided with restriction fragments capable of encoding known antigens, could express and purify the antigens of interest and employ these antigens to generate antigen-specific antibodies. Consequently, it is undisputed that appellants' claimed invention is enabled.

2. <u>Lack of Specific Response to Appellants' Arguments</u>

The Examiner did not specifically respond to Appellants' arguments in the Examiner's Answer, stating only that: "All issues raised by appellants have been fully responded to. For the above reasons, it is believed that the rejections should be sustained." (Examiner's Answer at 3.) The Examiner relies on Papers No. 31 and 34 as setting forth the grounds in support of the rejections. (*Id.*)

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Appellants respectfully submit that all issues raised by appellants in the Brief on Appeal have not been fully responded to since the grounds for rejection set forth in Papers No. 31 and 34 do not specifically address several of appellants' arguments. Rather, Papers No. 34 and 31 provide only general statements that, although broadly pertinent to appellants' arguments, do not respond to appellants' arguments with any specificity. Appellants and the Board are left to speculate how appellants' arguments have been addressed.

For example, in Paper No. 34, the Examiner alleged that the specification "fails to teach that the claimed restriction fragments encode the viral antigens of interest." (Paper No. 34 at 2.) Appellants' Brief addressed this issue. (*See* Brief at 9-11.) Appellants detailed how the specification describes that the claimed restriction fragments do encode viral antigens. Appellants further argued that it cannot be disputed that the claimed restriction fragments in the appealed claims do, in fact, encode antigens of the HIV-1 *gag*, *pol*, and *env* genes. (*See* Brief at 9.) The Examiner's general allegation in Paper No. 34 does not specifically respond to these arguments. Appellants can only speculate on the Office's position.

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In addition, appellants find no evidence in either Paper No. 31 or 34 that the Examiner even disputes that the claimed restriction fragments encode antigens of the *gag*, *pol*, and *env* genes. Rather, the Examiner has stated "Presumably these restriction fragments correspond to the *gag*, *pol*, and *env* genes." (Paper No. 31 at 2.) Consequently, that the claimed restriction fragments encode antigens of the *gag*, *pol*, and *env* genes does not even appear to be an issue.

In Paper No. 34, the Examiner also alleged that the specification "does not provide the nucleotide sequence of any of these restriction fragments, evidence that *bona fide* antigens were produced from said fragments, and evidence that antigen-specific antibodies were produced." (Paper No. 34 at 2-3.) The Examiner further alleged that the specification "fails to provide an adequate written description of method steps involving the production of an antigen from said restriction fragment, raising antibodies against said restriction fragment, and recovering antigen-specific antibodies." (Paper No. 34 at 3.) The Examiner also stated that the specification "fails to provide any demonstrative evidence that applicants had generated expression vectors containing the claimed inserts, transfected suitable hosts, and produced suitable levels of the recombinant

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proteins. . . [and] that these antigens were used to immunize animals and that HIV-1-specific antibodies were actually generated." (*Id.*) Appellants' Brief addressed all of these issues in great detail. (*See* Brief at 8-20.) Appellants can only speculate how their arguments were addressed prior to their presentation in the Brief.

For example, appellants explained that the claimed methods do not require any knowledge of nucleotide sequences to "describe" the antigens. (*See* Brief at 8-9.) The Examiner's general allegations in Paper No. 34 do not specifically respond to these arguments. Nowhere in Papers No. 31 or 34 is the Examiner's requirement for nucleotide sequence information explained. Consequently, appellants are unable to ascertain how their arguments have been addressed.

Furthermore, appellants pointed out how proteins and polypeptides encoded by the restriction fragments recited in the appealed claims are literally described in appellants' specification. (*See* Brief at 9-14.) Appellants detailed how the specification literally describes the use of these proteins and polypeptides as HIV-1 antigens. (*See* Brief at 12-14.) However, the Examiner has not specifically responded to these arguments.

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Again, appellants can only speculate how the Examiner's general assertions have addressed these arguments.

Appellants also detailed how the specification describes methods for the production of antigens from the claimed restriction fragments. (*See* Brief at 9-14.) Specifically, appellants pointed out how the specification provides an adequate description of the cloning of DNA fragments of the HIV-1 genome into expression vectors, expressing the DNA, and purifying the resulting proteins, and the use of proteins and polypeptides of the invention as antigens. (*See* Brief at 9-16.) However, the Examiner has not specifically responded to these arguments. Nowhere in Paper No. 31 or 34 does the Examiner specifically point out what is missing from this description. Nowhere is the Examiner's requirement for a working example of antigen production explained. Appellants are again left to speculate how their arguments have been addressed.

Furthermore, appellants detailed how the step of "raising antibodies" recited in claims 34, 35, and 36 is embodied in appellants' disclosure of the use of the HIV-1 proteins and polypeptides as "antigens" and "immunogens." (*See* Brief at 14-20.) Appellants pointed out that the specification's description of using appellants' proteins and polypeptides as "antigens" and "immunogens" provides a sufficient written description of the

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method step of "raising antibodies." (*Id.*) However, the Examiner has not specifically responded to these arguments. Appellants are once more left to speculate how their arguments have been addressed.

In conclusion, appellants presented detailed arguments that the claimed invention was fully described in the specification despite the contentions of the Examiner. Appellants' arguments addressed all of the Examiner's grounds for rejection in great detail. However, the Examiner has not specifically responded to these arguments, but has simply referred to previous general allegations. Appellants submit that the Examiner's lack of specific response to their arguments evidences the incontrovertibility of these arguments.

Reversal of the rejection the claims under 35 U.S.C. § 112, first paragraph, on the ground of lack of an adequate written description is respectfully requested.

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Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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